EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

8 December 2022

COVID-19 vaccines safety update

Comirnaty (BioNTech Manufacturing GmbH)
COVID-19 Vaccine Valneva (Valneva Austria GmbH)
Jcovden (Janssen-Cilag International NV)
Nuvaxovid (Novavax CZ, a.s.)
Spikevax (Moderna Biotech Spain, S.L.)
Vaxzevria (AstraZeneca AB)
VidPrevtyn Beta (Sanofi Pasteur)

The safety of authorised COVID-19 vaccines is continuously monitored, and updated information is regularly provided to the public.

Safety updates outline the outcomes from assessments of emerging worldwide safety data carried out mainly by EMA's Pharmacovigilance Risk Assessment Committee (PRAC) (section 1). They also outline how safety is monitored and contain high-level information on suspected adverse reaction reports, which PRAC takes into account in its assessments (section 2).

This safety update follows the update of 10 November 2022 and reflects the main assessment outcomes of the PRAC meeting held from 28 November to 1 December 2022.

EMA confirms that the benefits of all currently authorised COVID-19 vaccines continue to outweigh their side effects, given the risk of COVID-19 illness and related complications, including hospitalisation and death.

EMA will cease the publication of monthly safety updates for COVID-19 vaccines with this safety update of December 2022.

The wide uptake of COVID-19 vaccines in immunisation programmes during the pandemic emergency led to a rapid accumulation of extensive safety data from spontaneous reports of suspected adverse reactions. Since the first vaccines were authorised in December 2020, EMA's monthly safety

updates have provided information on the assessment of these reports and data from other sources.

The majority of the EU population has now received at least one COVID-19 vaccine[1]; data from clinical trials, other studies and spontaneous reporting have established the safety profiles of these vaccines.

As for all medicines authorised in the EU, safety monitoring and timely assessment of emerging data will continue for the COVID-19 vaccines. If there are any major safety-related changes to the existing product information for any COVID-19 vaccine, these will be communicated in the PRAC highlights, together with dedicated public health communications as needed. For each vaccine, all identified side effects are listed in the relevant product information in all the languages of the European Union (EU)/European Economic Area (EEA) (see section 1). High-level information on suspected adverse reaction reports will continue to be updated monthly on EMA's webpage on COVID-19 vaccines. The website EudraVigilance – European database of suspected drug reaction reports will continue to be updated weekly.

Key messages from the latest safety assessments

No updates are currently needed to the product information of any of the authorised COVID-19 vaccines.

1. Latest safety assessments

Comirnaty (BioNTech Manufacturing GmbH)

Based on continuous safety monitoring and assessments, there are currently no updates to the product information of Comirnaty.

[1] The European Centre for Disease Prevention and Control (ECDC) collects these exposure data from EU Member States as well as from the additional countries of the European Economic Area (EEA) Norway, Iceland and Liechtenstein.

About 685 million doses of Comirnaty original vaccine, including about 57.3 million doses in children and adolescents (below 18 years of age), were administered in the EU/EEA from authorisation to 13 November 2022.

Additionally, about **16.1 million doses of adapted bivalent Comirnaty vaccines, including about 52,400 doses in adolescents (below 18 years of age)**, have been administered.[2]

The initial conditional marketing authorisation for Comirnaty in the EU was issued on 21 December 2020. Following an assessment process, it was converted into a standard marketing authorisation on 10 October 2022. Information on how Comirnaty works is provided in the medicine overview (in all EU/EEA languages). Full information on the vaccine, including all identified side effects and advice on how to use it, is available in the product information (in all EU/EEA languages).

COVID-19 Vaccine (inactivated, adjuvanted) Valneva (Valneva Austria GmbH)

Based on continuous safety monitoring and assessments, there are currently no updates to the product information of COVID-19 Vaccine (inactivated, adjuvanted) Valneva.

About 2,900 doses of COVID-19 Vaccine (inactivated, adjuvanted) Valneva in adults were administered in the EU/EEA from authorisation to 13 November 2022.[2]

The initial, standard marketing authorisation for COVID-19 Vaccine (inactivated, adjuvanted) Valneva in the EU was issued on 24 June 2022. Information on how COVID-19 Vaccine (inactivated, adjuvanted) Valneva works is provided in the medicine overview (in all EU/EEA languages). Full information on the vaccine, including all identified side effects and advice on how to use it, is available in the product information (in all EU/EEA languages).

[2] The European Centre for Disease Prevention and Control (ECDC) collects these exposure data from EU Member States as well as from the additional countries of the European Economic Area (EEA) Norway, Iceland and Liechtenstein.

Jcovden (Janssen-Cilag International NV)

Based on continuous safety monitoring and assessments, there are currently no updates to the product information of Jcovden.

About 18.6 million doses of Jcovden in adults were administered in the EU/EEA from authorisation to 13 November 2022.[3]

The initial conditional marketing authorisation for Jcovden (previously COVID-19 Vaccine Janssen) in the EU was issued on 11 March 2021. Information on how Jcovden works is provided in the medicine overview (in all EU/EEA languages). Full information on the vaccine, including all identified side effects and advice on how to use it, is available in the product information (in all EU/EEA languages).

Nuvaxovid (Novavax CZ, a.s.)

Based on continuous safety monitoring and assessments, there are currently no updates to the product information of Nuvaxovid.

About 361,300 doses of Nuvaxovid in adults were administered in the EU/EEA from authorisation to 13 November 2022.[3]

The initial conditional marketing authorisation for Nuvaxovid in the EU was issued on 20 December 2021. Information on how Nuvaxovid works is provided in the medicine overview (in all EU/EEA languages). Full information on the vaccine, including all identified side effects and advice on how to use it, is available in the product information (in all EU/EEA languages).

[3] The European Centre for Disease Prevention and Control (ECDC) collects these exposure data from EU Member States as well as from the additional countries of the European Economic Area (EEA) Norway, Iceland and Liechtenstein.

Spikevax (Moderna Biotech Spain, S.L.)

Based on continuous safety monitoring and assessments, there are currently no updates to the product information of Spikevax.

About 161 million doses of Spikevax original vaccine, including about 3.1 million doses in children and adolescents (below 18 years of age), were administered in the EU/EEA from authorisation to 13 November 2022.

Additionally, about **317,800 doses of adapted bivalent Spikevax vaccines, including about 200 doses in adolescents (below 18 years of age)**, have been administered.[4]

The initial conditional marketing authorisation for Spikevax (previously COVID-19 Vaccine Moderna) in the EU was issued on 06 January 2021. Following an assessment process, it was converted into a standard marketing authorisation on 03 October 2022. Information on how Spikevax works is provided in the medicine overview (in all EU/EEA languages). Full information on the vaccine, including all identified side effects and advice on how to use it, is available in the product information (in all EU/EEA languages).

Vaxzevria (AstraZeneca AB)

Based on continuous safety monitoring and assessments, there are currently no updates to the product information of Vaxzevria.

About 68.8 million doses of Vaxzevria in adults were administered in the EU/EEA from authorisation to 13 November 2022.[4]

The initial conditional marketing authorisation for Vaxzevria (previously COVID-19 Vaccine AstraZeneca) in the EU was issued on 29 January 2021. Following an assessment process, it was converted into a standard marketing authorisation on 31 October 2022. Information on how Vaxzevria works is provided in the medicine overview (in all EU/EEA languages). Full information on the vaccine, including all identified side effects and advice on

[4] The European Centre for Disease Prevention and Control (ECDC) collects these exposure data from EU Member States as well as from the additional countries of the European Economic Area (EEA) Norway, Iceland and Liechtenstein.

how to use it, is available in the product information (in all EU/EEA languages).

VidPrevtyn Beta (Sanofi Pasteur)

There are no safety updates for VidPrevtyn Beta, which was recently authorised and has not yet been used in the EU/EEA[5].

The initial, standard marketing authorisation for VidPrevtyn Beta in the EU was issued on 10 November 2022. Information on how VidPrevtyn Beta works is provided in the medicine overview (in all EU/EEA languages). Full information on the vaccine, including all identified side effects and advice on how to use it, is available in the product information (in all EU/EEA languages).

2. How safety is monitored

Before COVID-19 vaccines were granted EU marketing authorisation, the efficacy and safety of the vaccines were assessed in pre-clinical studies and large clinical trials.

All relevant new information emerging worldwide on the vaccines since marketing authorisation is collected and promptly assessed. This is in line with the pharmacovigilance plan for COVID-19 vaccines of the EU regulatory network (comprising the regulatory bodies of the EU Member States, EMA and the European Commission).

EMA's detailed assessments take into account all available data from all sources to draw robust conclusions on the safety of the vaccines. These data include clinical trial results, reports of suspected side effects, epidemiological studies monitoring the safety of the vaccine, toxicological investigations and any other relevant information.

Summary safety reports

The pharmacovigilance plan for COVID-19 vaccines includes monthly summary safety reports (MSSRs) which are compiled by the marketing authorisation holders to support timely and continuous benefit-risk evaluations for COVID-19 vaccines used during the pandemic. MSSRs are intended to be compiled in the first months of marketing. Afterwards, summary safety reports may cover time periods longer than a month or

[5] The European Centre for Disease Prevention and Control (ECDC) collects these exposure data from EU Member States as well as from the additional countries of the European Economic Area (EEA) Norway, Iceland and Liechtenstein.

may not be necessary anymore. Summary safety reports complement periodic safety update reports (PSURs).

Case reports of suspected side effects

Collecting reports of medical events and problems that occur following the use of a medicine, and therefore might be side effects, is one of the pillars of the EU safety monitoring system.

Healthcare professionals and vaccinated individuals are encouraged to report to their national competent authorities all suspected side effects individuals may have experienced after receiving a vaccine even if it is unclear whether the vaccine was the cause. For more information on how to report, including the importance of detailing the vaccine product name and the batch, see Reporting suspected side effects.

These spontaneous reports are collected in EudraVigilance, the EU database used for monitoring and analysing suspected side effects. Publicly available information can be accessed via the website EudraVigilance – European database of suspected drug reaction reports (in all EU/EEA languages).

As of 23 November 2022, EudraVigilance contained the following:

- Comirnaty: a total of 967,351 cases (plus 3,670 cases for Comirnaty adapted bivalent vaccines) of suspected side effects spontaneously reported from EU/EEA countries; 8,368 of these reported a fatal outcome (plus 51 for Comirnaty adapted bivalent vaccines)[6,7] (by 13 November 2022, about 685 million doses of Comirnaty original vaccine and about 16.1 million doses of Comirnaty adapted bivalent vaccines had been given to people in the EU/EEA[8]);
- COVID-19 Vaccine (inactivated, adjuvanted) Valneva: 24 case of suspected side effects spontaneously reported from EU/EEA countries; none reported a fatal outcome[6,7] (by 13 November 2022, about 2,900 doses of COVID-19 Vaccine (inactivated, adjuvanted) Valneva had been given to people in the EU/EEA[8]);
- Jcovden: a total of 58,223 cases of suspected side effects spontaneously reported from EU/EEA countries; 339 of these reported a fatal outcome[6,7] (by 13 November 2022, about 18.6 million doses of Jcovden had been administered to people in the EU/EEA[8]);

[6] These figures have been calculated excluding cases reported from Northern Ireland (EU reporting requirements for suspected adverse reactions to EudraVigilance apply to Northern Ireland in accordance with the Protocol on Ireland/Northern Ireland).

[7] Source: EudraVigilance. These figures cannot be extracted directly from the public database of suspected adverse reactions, which groups information per type of side effect. As more than one suspected side effect may have been included in a single case report, the total number of side effects will never match the number of individual cases. Similarly, this public database does not provide the total number of cases reported with a fatal outcome.

[8] The European Centre for Disease Prevention and Control (ECDC) collects these exposure data from EU Member States as well as from the additional countries of the European Economic Area (EEA) Norway, Iceland and Liechtenstein.

- Nuvaxovid: a total of 1,423 cases of suspected side effects spontaneously reported from EU/EEA countries; 1 reported a fatal outcome[9,10] (by 13 November 2022, about 361,300 doses of Nuvaxovid had been administered to people in the EU/EEA[11]);
- Spikevax: a total of 270,827 cases (plus 3,120 cases for Spikevax adapted bivalent vaccines) of suspected side effects spontaneously reported from EU/EEA countries; 1,161 of these reported a fatal outcome (plus 16 for Spikevax adapted bivalent products)[9,10] (by 13 November 2022, about 161 million doses of Spikevax original vaccine and about 317,800 doses of Spikevax adapted bivalent vaccines had been given to people in the EU/EEA[11]);
- Vaxzevria: a total of 328,643 cases of suspected side effects spontaneously reported from EU/EEA countries; 1,579 of these reported a fatal outcome[9,10] (by 13 November 2022, about 68.8 million doses of Vaxzevria had been given to people in the EU/EEA[11]);
- VidPrevtyn Beta: no cases of suspected side effects spontaneously reported from EU/EEA countries[9,10] (by 13 November 2022, the vaccine had not yet been used in the EU/EEA[11]).

These reports describe suspected side effects in individuals, i.e. medical events observed following the use of a vaccine. The fact that someone has had a medical issue or died after vaccination does not necessarily mean that this was caused by the vaccine. This may have been caused, for example, by health problems not related to the vaccination.

The EU regulatory network continuously monitors EudraVigilance to detect any new safety issues. EudraVigilance relies on individual healthcare professionals and patients to report their own experience. The monitoring detects unusual or unexpected patterns in the reports received for further investigation and risk assessment.

Planned and ongoing studies

The companies that market COVID-19 vaccines continue to provide results from ongoing clinical trials. They also conduct additional studies to monitor the safety and effectiveness of the vaccines as they are used in vaccination campaigns and other clinical practice. For the list of planned and ongoing

[9] These figures have been calculated excluding cases reported from Northern Ireland (EU reporting requirements for suspected adverse reactions to EudraVigilance apply to Northern Ireland in accordance with the Protocol on Ireland/Northern Ireland).

[10] Source: EudraVigilance. These figures cannot be extracted directly from the public database of suspected adverse reactions, which groups information per type of side effect. As more than one suspected side effect may have been included in a single case report, the total number of side effects will never match the number of individual cases. Similarly, this public database does not provide the total number of cases reported with a fatal outcome.

[11] The European Centre for Disease Prevention and Control (ECDC) collects these exposure data from EU Member States as well as from the additional countries of the European Economic Area (EEA) Norway, Iceland and Liechtenstein.

safety studies, see the respective risk management plan (RMP) for Comirnaty, COVID-19 Vaccine (inactivated, adjuvanted) Valneva, Jcovden, Nuvaxovid, Spikevax, Vaxzevria and VidPrevtyn Beta.

A paediatric investigation plan (PIP) is in place for Comirnaty, COVID-19 Vaccine (inactivated, adjuvanted) Valneva, Jcovden, Nuvaxovid, Spikevax and Vaxzevria. The PIP describes how the company will collect data on the vaccine's efficacy and safety for its potential use in children and adolescents (below 18 years of age). Three vaccines are authorised in the EU for use in children and adolescents: Comirnaty (as of 6 months; adapted bivalent vaccines as of 12 years), Nuvaxovid (as of 12 years) and Spikevax (as of 6 months; adapted bivalent vaccines as of 12 years).

In addition, EMA is coordinating observational studies in EU Member States looking at real-world data from clinical practice to monitor the safety and effectiveness of COVID-19 vaccines, including in pregnant women.

European Medicines Agency

Official address Domenico Scarlattilaan 6 ● 1083 HS Amsterdam ● The Netherlands

Address for visits and deliveries Refer to www.ema.europa.eu/how-to-find-us

Send us a question Go to www.ema.europa.eu/contact

Telephone +31 (0)88 781 6000

© European Medicines Agency, 2022. Reproduction is authorised provided the source is acknowledged.

An agency of the European Union